

1 ATGGGGCCAC CACCAGCTAG AGTACATCTA GGTGCTTTCC TGGCAGTGAC TCCGAATCCC GGGAGCGCAG CCAGTGGGAC AGAGGCAGCC GCGGCCACAC
TACCGGGGTG GTGGTCGATC TCATGTAGAT CCACGCAAGG ACGTCACTG AGGCTTAGGG CCCTCGCGTC GCTCACCTG TCTCCGTGG GCGCGGTGTG
1 MetAlaProp roProAlaAr gValHisLeu GlyAlaPheL euAlaValTh rProAsnPro GlySerAlaA laSerGlyTh rGluAlaAla AlaAlaThrPro
101 CCAGCAAAGT GTGGGGCTCT TCCGCGGGGA GGATTGAACC ACGAGGCGGG GCGCGAGGAG CGCTCCCTAC CTCCATGGGA CAGCAGGAC CCAGTGCCTG
GGTCGTTTCA CACCCCGAGA AGCGGCCCTT CCTAACTTGG TGCTCCGCC CCGGCTCCTC GCGAGGATG GAGGTACCTT GTCGTGCCTG GGTACAGGGC
35 SerLysva lTrpGlySer SerAlaGlyA rgileGluPr oArgGlyGly GlyArgGlyA laLeuProTh rSerMetGly GlnHisGlyP roSerAlaArg
201 GGCCCGGGCA GGGCGCGCCC CAGGACCCAG GCGCGCGGG GAAGCCAGCC CTCGGCTCCG GGTCCACAAG ACCTTCAAGT TTGTCGTCGT CCGGGTCTCTG
CCGGGCCCGT CCGCGCGGG GTCTGGGTG GTCTGGGTG CCGCGCGGCC CTTCGGTCGG GAGCCGAGG CCAGGTGTTT TGAAGTTCA AACACGACCA GCGCCAGGAC
68 AlaArgAla GlyArgAlap roGlyProAr gProAlaArg GluAlaSerP roArgLeuAr gValHisLys ThrPheLysP heValValva lGlyValLeu
301 CTGCAGGTCT TACCTAGCTC AGCTGCAACC ATCAAACTTC ATGATCAATC AATTGGCACA CAGCAATGGG AACATAGCCC TTGGGAGAG TTGTGTCAC
GAGTCCAGC ATGGATCGAG TCGACGTTGG TAGTTTGAAG TACTAGTTAG TTAACCGTGT GTCGTTACCC TTGTATCGGG AAACCTCTC AACACAGGTG
101 LeuGlnValv alProSerse rAlaAlaThr ileLysLeuH isAspGlnSe rileGlyThr GlnGlnTrpG luHisSerPr oLeuGlyGlu LeuCysProPro
401 CAGGATCTCA TAGATCAGAA CGTCTGGAG CCTGTAACCG GTGCACAGAG GGTGTGGGT ACACCAATGC TTCCAACAAT TTGTTGCTT GCCTCCCATG
GTCCTAGAGT ATCTAGTCTT GCAGGACCTC GGACATTGGC CACGTGTCTC CCACACCCAA TGTGTTTACG AAGGTTGTTA AACAAACGAA CCGAGGGTAC
135 GlySerHI sArgSerGlu ArgProGlyA lacysAsnAr gCysThrGlu GlyValGlyT yThrAsnAl aSerAsnAsn LeupheAlaC ysLeuProCys
501 TACAGCTTGT AAATCAGATG AAGAAGAGAG AAGTCCCTGC ACCACGACCA GGAACACAGC ATGTCAGTGC AAACCAGGAA CTTTCCGGAA TGACAATTCT
ATGTCGAACA TTTAGTCTAC TTCTTCTCTC TTCAGGGACG TGGTGTGTT CTTGTGTGTC TACAGTCACG TTTGTCCTT GAAAGGCTT ACTGTTAAGA
168 ThrAlaCys LysSerAspG luGluGluAr gSerProCys ThrThrThra rAsnThraI acysGlnCys LysProGlyT hrPheArgAs naspsnSer
601 GCTCAGATGT GCCGGAAGTG CAGCACAGG TGCCCCAGAG GGATGGTCAA GGTCAAGGAT TGTAAGCCCT GTAGTGACAT CGAGTGTGTC -CACAAAGAA
CGACTCPAC CCGCCTTAC GTCGTGTC CCGGGTCTC ACGGGTCTC CTACACAGT CCAGTTCTTA ACATGCGGA CCTCACTGTA GCTCACACAG GTGTTTCTTA
201 AlaGluMetc ysArgLysCy sSerThrGly CysProArgG lyMetVally svalLysAsp CysThrProT rpSerAspIl eGluCysVal HisLysGluSer
701 CAGGCAATGG ACATAATATA TGGGTGATTT TGGTTGTGAC TTTGTTGTTT CCGTTGCTGT TGGTGGCTGT GCTGATTGTC TGTGTTGCA TCGGCTCAGG
GTCGTTTACC TGTATTATAT ACCCACTAAA ACCAACACTG AACCAACAA GGCACGACA ACCACCGACA CGACTAACAG ACAACAACGT AGCCGAGTCC
235 GlyAsnGl yHisAsnIle TrpValIleL euValValTh rLeuValVal ProLeuLeuL euValAlaVa lLeuIleVal CysCysCysI leGlySerGly
801 TTGTGGAGGG GACCCCAAGT GCATGGACAG GGTGTGTTTC TGGCGTTTG GTCTCTACG AGGCGCTGG GCTGAGGACA ATGCTCACAA CGAGATTCTG
AACACTCCC CTGGGGTTCA CGTACCTGTC CCACACAAAG ACCGCGAACC CAGAGGATGC TCCCGGACCC CGACTCCTGT TACGAGTGTG GCTCTAAGAC
268 CysGlyGly AspProLysC ysMetAspAr gValCysPhe TrpArgLeuG lyLeuLeuAr gGlyProGly AlaGluAspA snAlaHisAs nglulleLeu
901 AGCAACGCAG ACTCGCTGTC CACTTTCGTC TCTGACGAC AATGGAAAG CCAGGAGCCG GCAGATTGTA CAGGTGTAC TGTACAGTCC CCAGGGGAGG
TCGTTGCGTC TGAGCGACAG GTGAAAGCAG AGACTCGTGC TTTACCTTTC GGTCCTCGG CGTCTAACT GTCCACAGTG ACATGTACAG GGTCCCTCC
301 SerAsnAlaA spSerLeuse rThrPheVal SerGluGlnG lnMetGluse rGlnGluPro AlaAspLeuT hrGlyValTh rValGlnSer ProGlyGluAla
1001 CACAGTGTCT GCTGGGACCG GCAGAAGCTG AAGGCTCTCA GAGGAGGAG CTGCTGGTTC CAGCAAATGG TGCTGACCCC ACTGAGACTC TGATGCTGTT
GTGTCACAGA CGACCTGGC GGTCTTCGAC TTCCACAGAT CTCCTCTCC CAGCACCAAG GTCGTTTACC ACGACTGGG TGACTCTGAG ACTACGACAA
335 GlnCysLe uLeuGlyPro AlaGluAlag luGlySerGl narArgArg LeuLeuValP roAlaAsnGl yAlaAspPro ThrGluThrL euMetLeuphe

Fig. 1

1101 CTTTGACAAG TTTGCAAAACA TCGTGGCCCTTT TGACTTCCTGG GACCAGGCTCA TGAGGCAGCTT GGACCTCAGG AAAAATGAGA TCGATGTGGT CAGAGCTGGT
 GAAACTGTTT AAACGTTTGT AGCAGCGGAA ACTGAGGAGG ACCTCCGTCGA CCTGGAGTGC TTTTACTCT AGCTACACCA GTCTCGACCA
 368 PheAspLys PheAlaAsnI leValProPh eAspGluTyr AspGlnLeuM etArgGlnLe uAspLeuThr LysAsnGluI leAspValVa lArgAlaGly
 1201 ACAGCAGGCC CAGGGGATGC CTGTATGCA ATGCTGATGA AATGGGTCAA CAAAACCTGGA CGAATCCACAC CCTGCTGGAT GCCTTGGAGA
 TGTCGTCCGG GTCCCCCTACG GAACATACGT TACGACTACT TTACCCAGTT GTTTGGACCT GCCTTGCGGA GCTAGGTGTG GGACGACCTA CGGAACCTCT
 401 ThrAlaGlyP roGlyAspAl aLeuTyrAla MetLeuMetL yStrpValAs nLysThrGly ArgAsnAlas erIleHisTh rLeuLeuAsp AlaLeuGluArg
 1301 GGATGGAAGA GAGACATGCA AAAGACAAGA TTCAGGACCT CTTGGTGGAC TCTGGAAAGT TCATCTACTT AGAAGATGGC ACAGGCTCTG CCGTGTCTCT
 CCTACCTTCT CTCTGTACGT TTTCTCTTCT AAGTCCCTGA GAACCCCTG AGACCTTTCA AGTAGATGAA TCTTCTACCG TGTCGAGAC GGCACAGGAA
 435 MetGluG1 uArgHisAla LysGluLysI leGlnAspLe uLeuValAsp serGlyLysP heIleTyrLe uGluAspGly ThrGlySera laValSerLeu
 1401 GGAGTGA
 CCTCACT
 468 GluOP*

Fig. 1 (cont.)

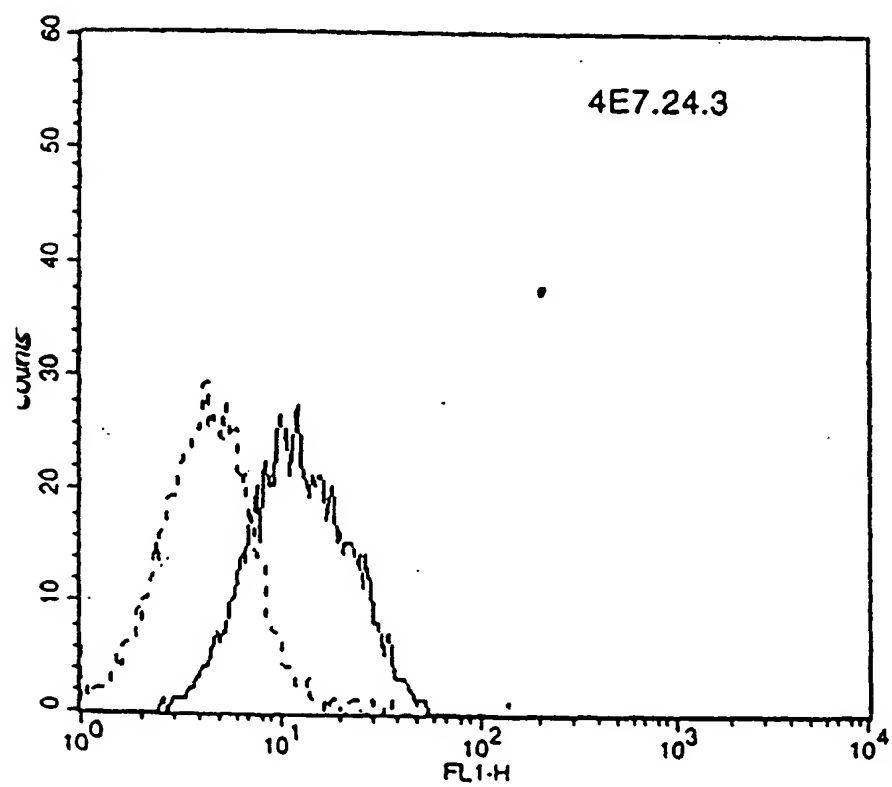
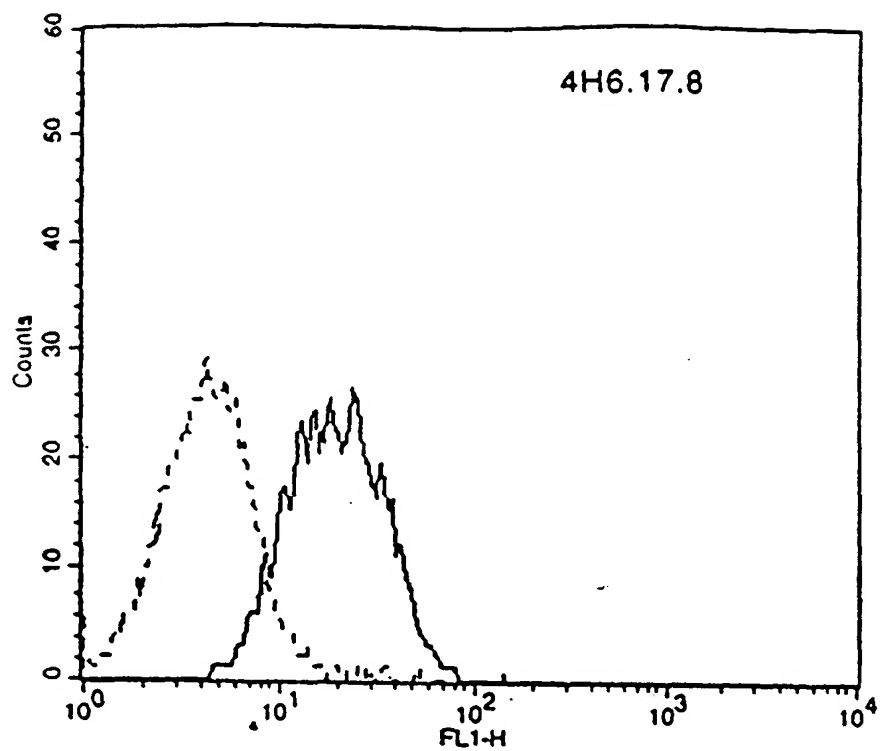


Fig. 2

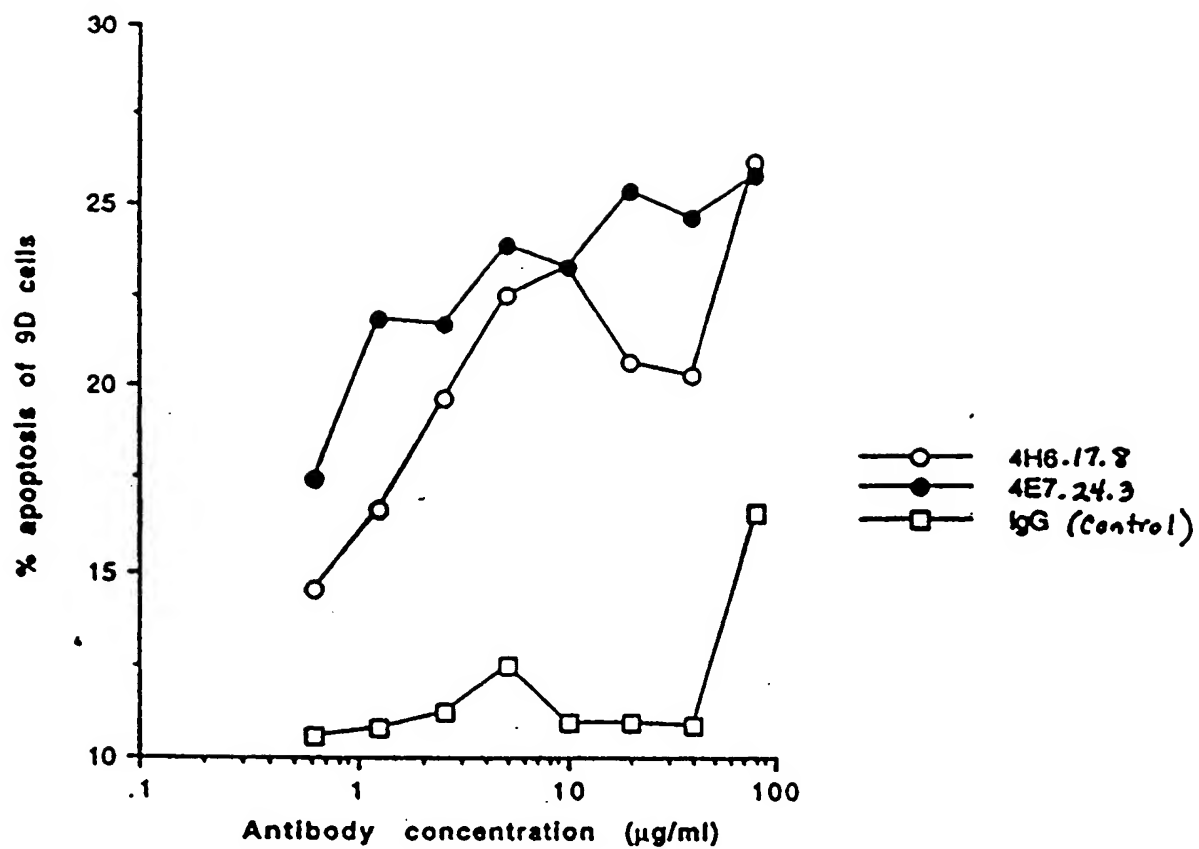


Fig. 3

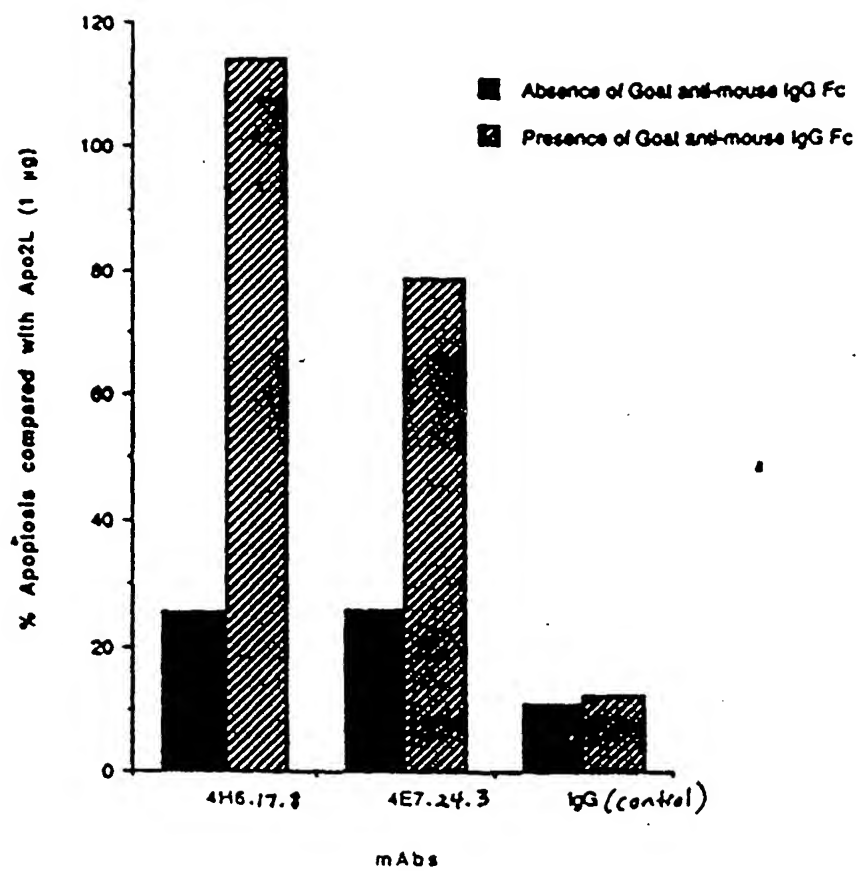


Fig. 4

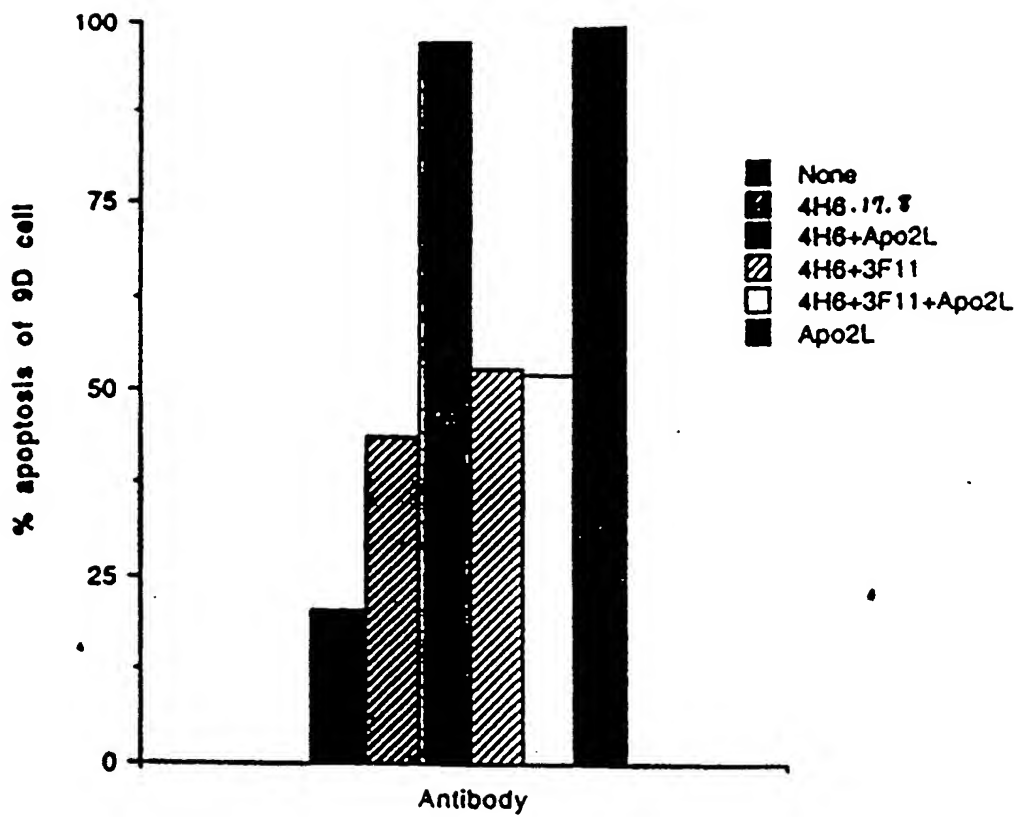
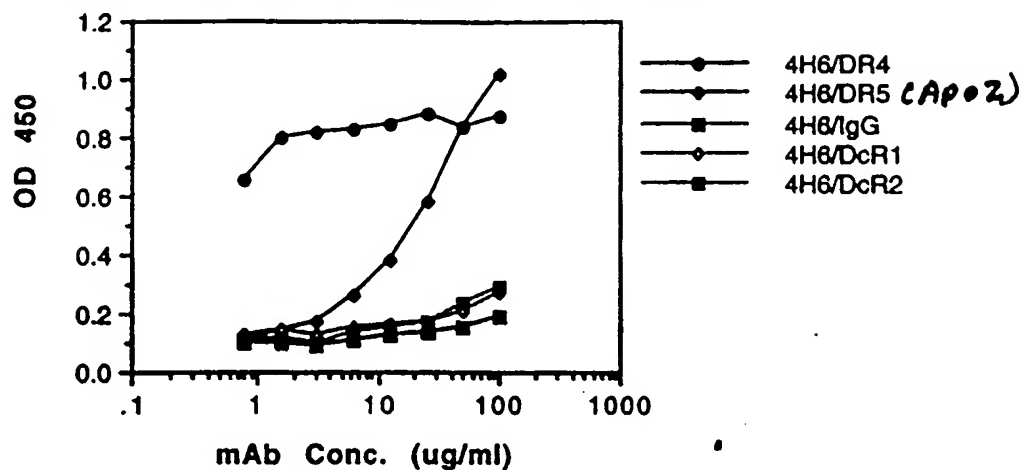


Fig. 5

4H6: Binding to receptors for Apo2L



4E7: Binding to Receptors for Apo2L

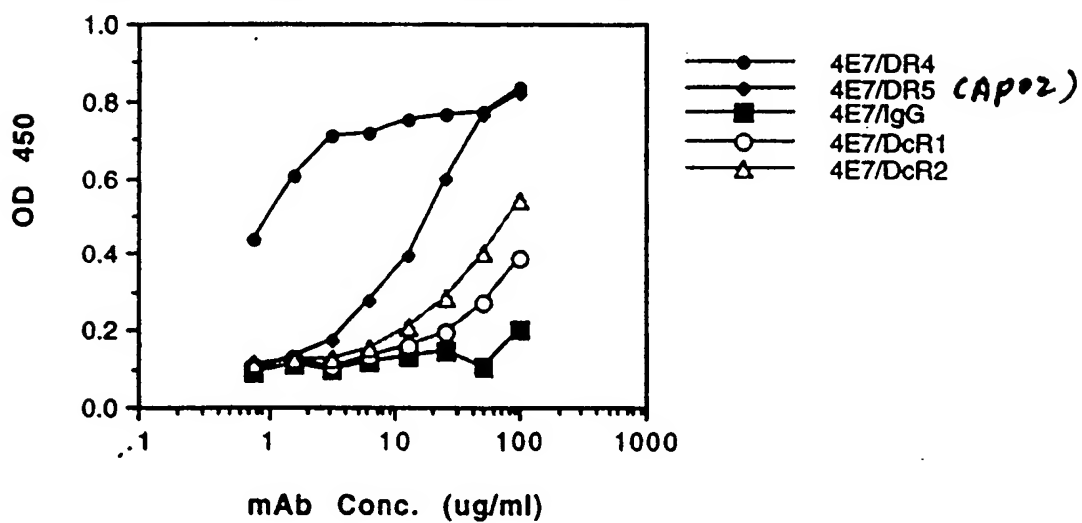


Fig. 6

Affinities of Apo2Rs and mAbs

		Affinity (pM)
DR4-IgG	to Apo2L	82
DR5-IgG	to Apo2L	1
mAb 4E7	to DR4-IgG	2
mAb 4H6	to "	5
mAb 5G11	to "	22
mAb 3F11	to DR5-IgG	20
mAb 3H3	to "	3

Affinities were determined using KinExA

Fig. 7

Apoptosis of 9D cells by anti-DR4 mAbs plus complements or goat anti-mouse Ig-Fc

Percent Apoptosis compared to Apo2L

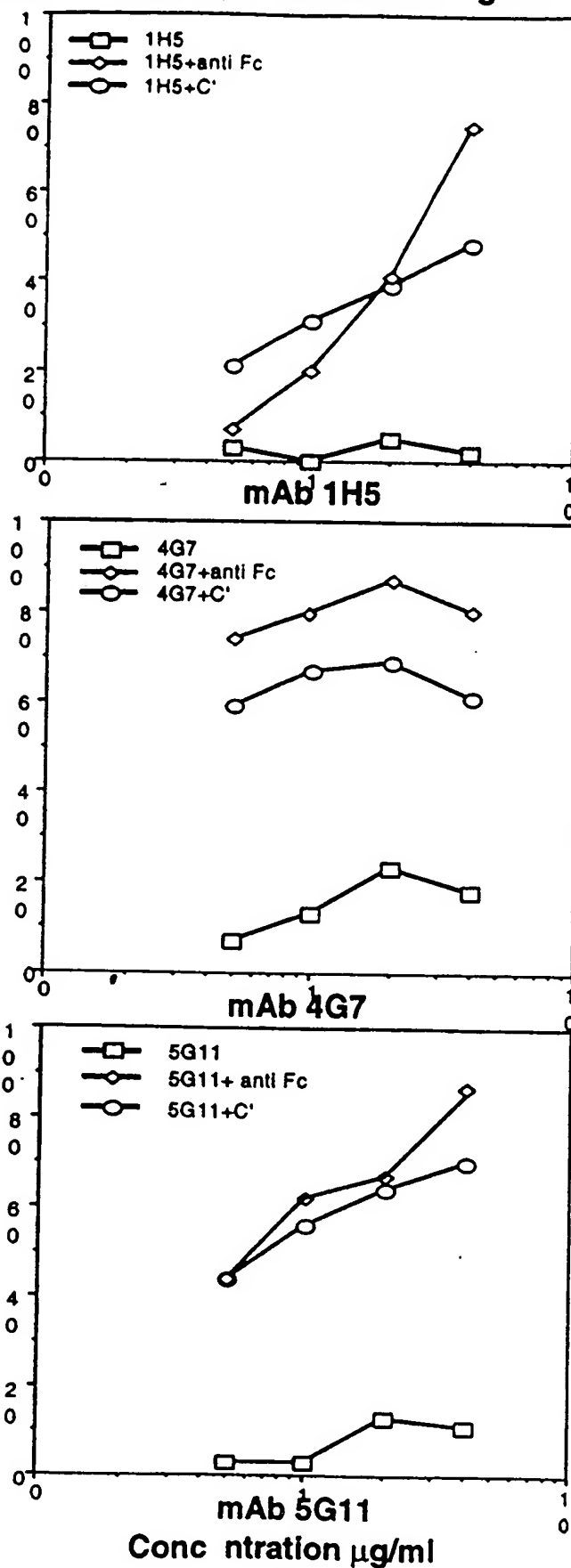


Fig. 8A

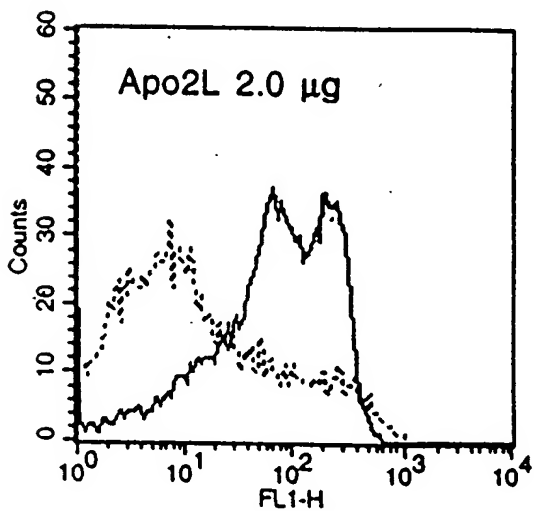
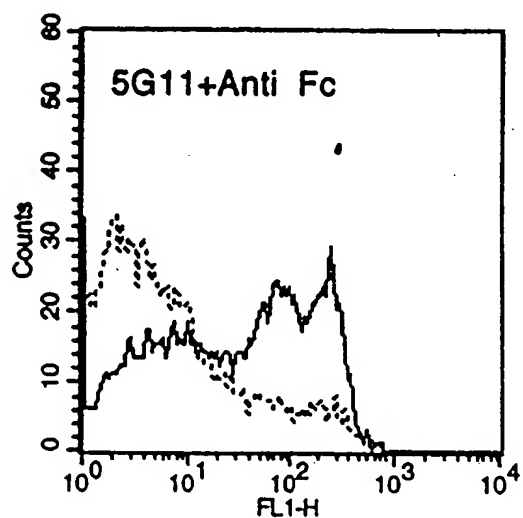
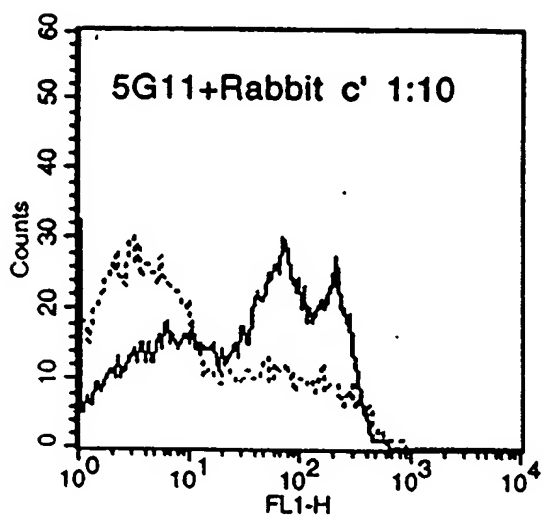
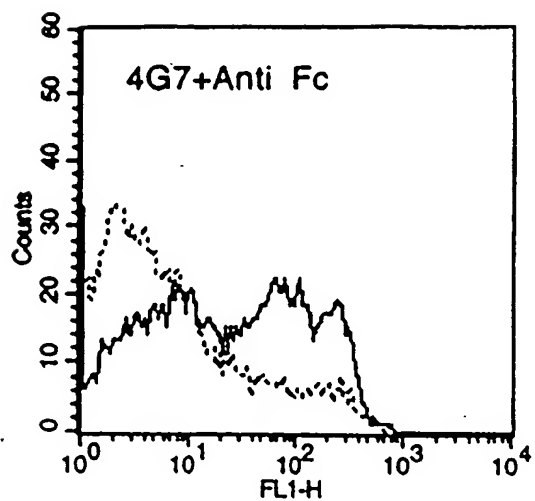
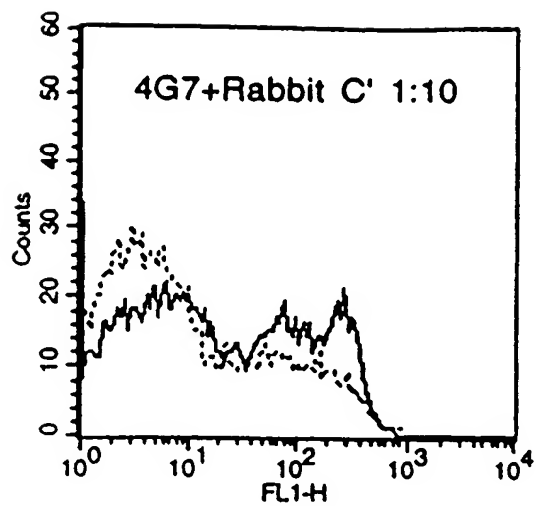
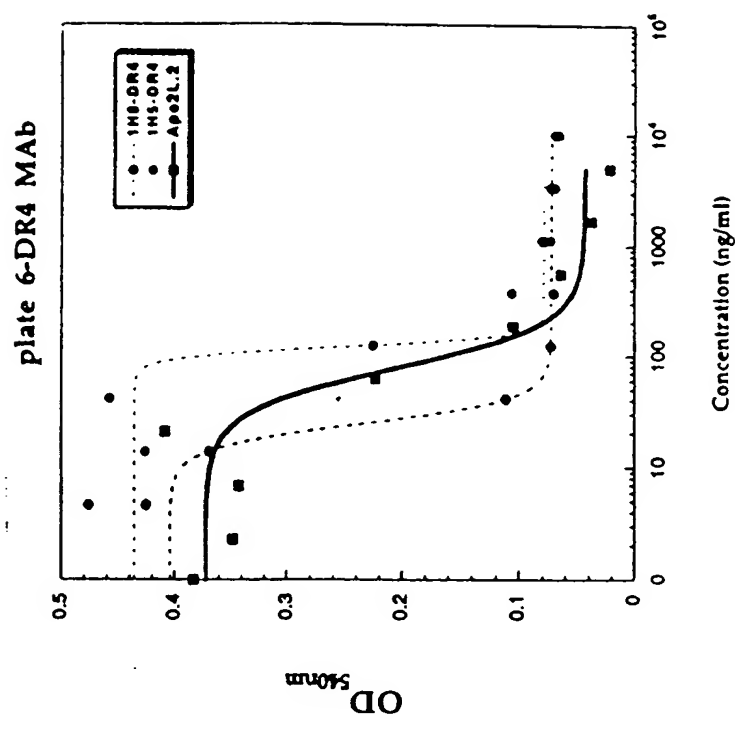
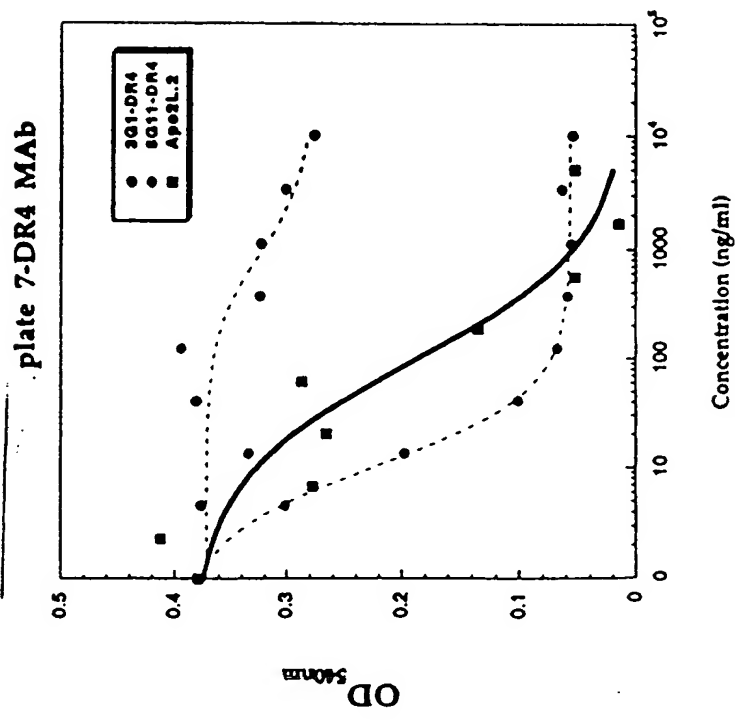
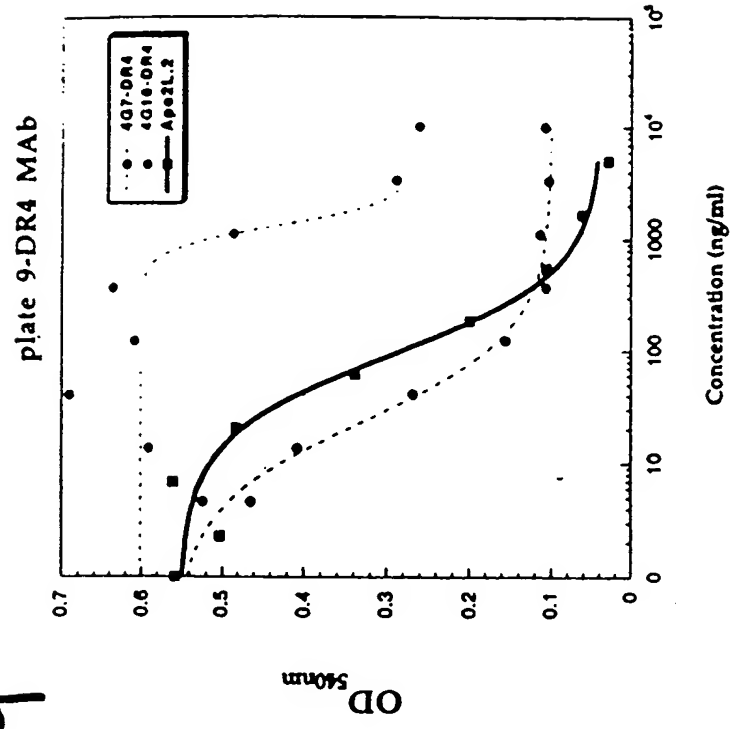
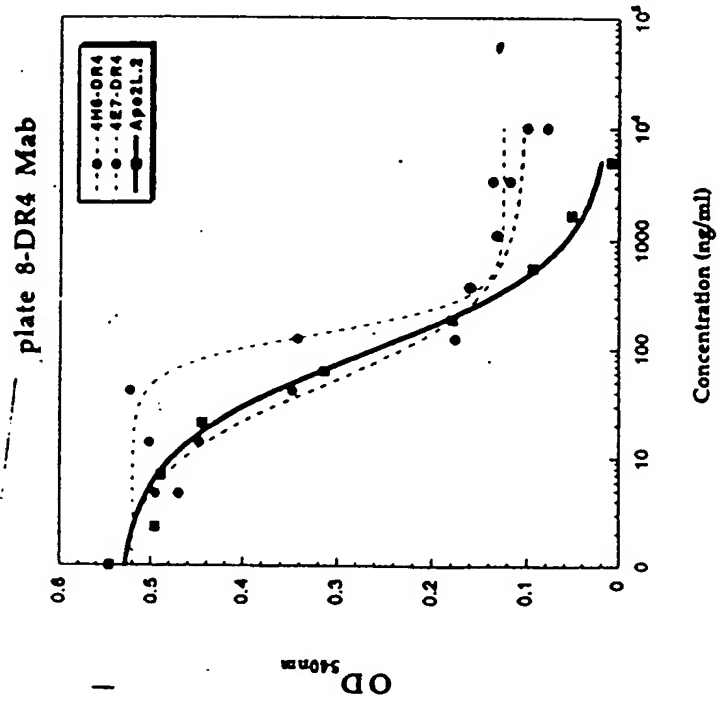
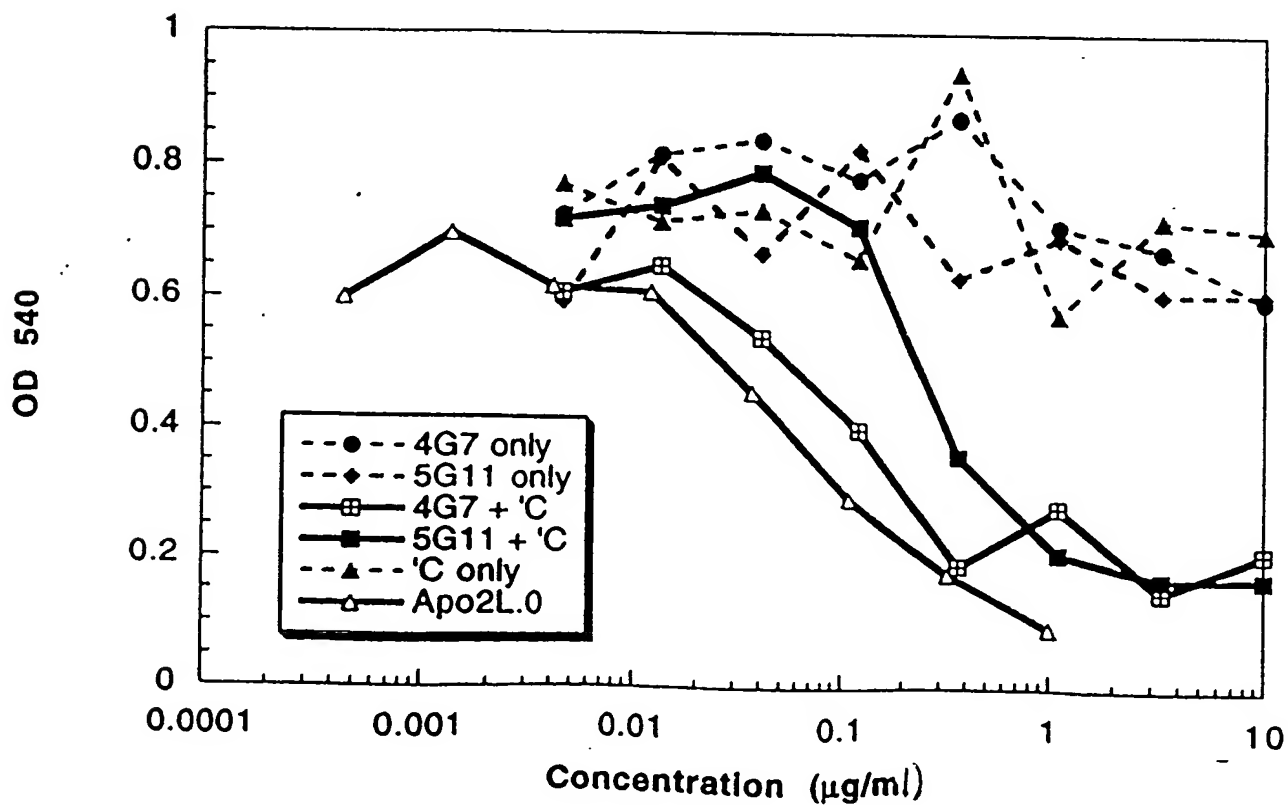
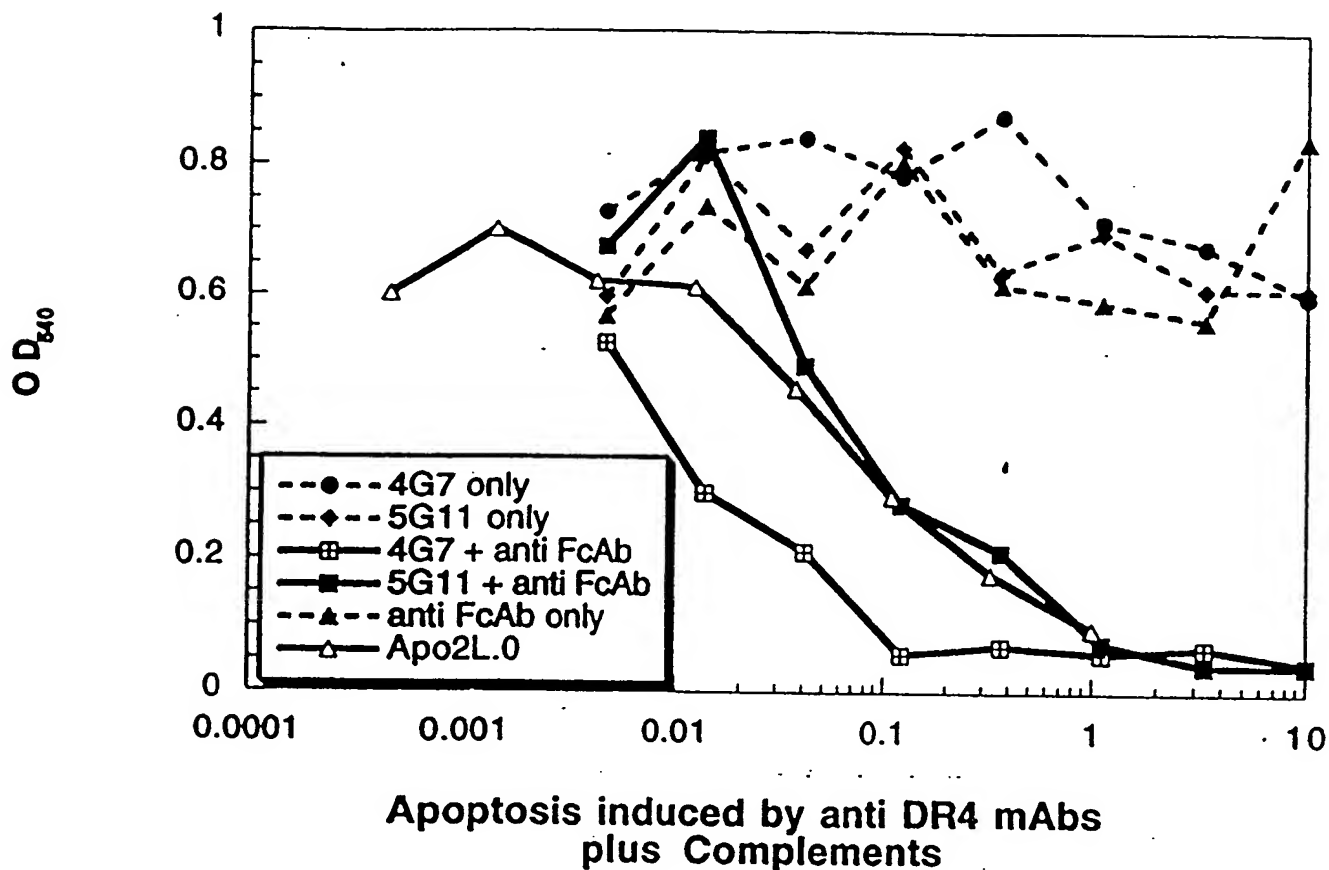


Fig. 8B

Fig. 9

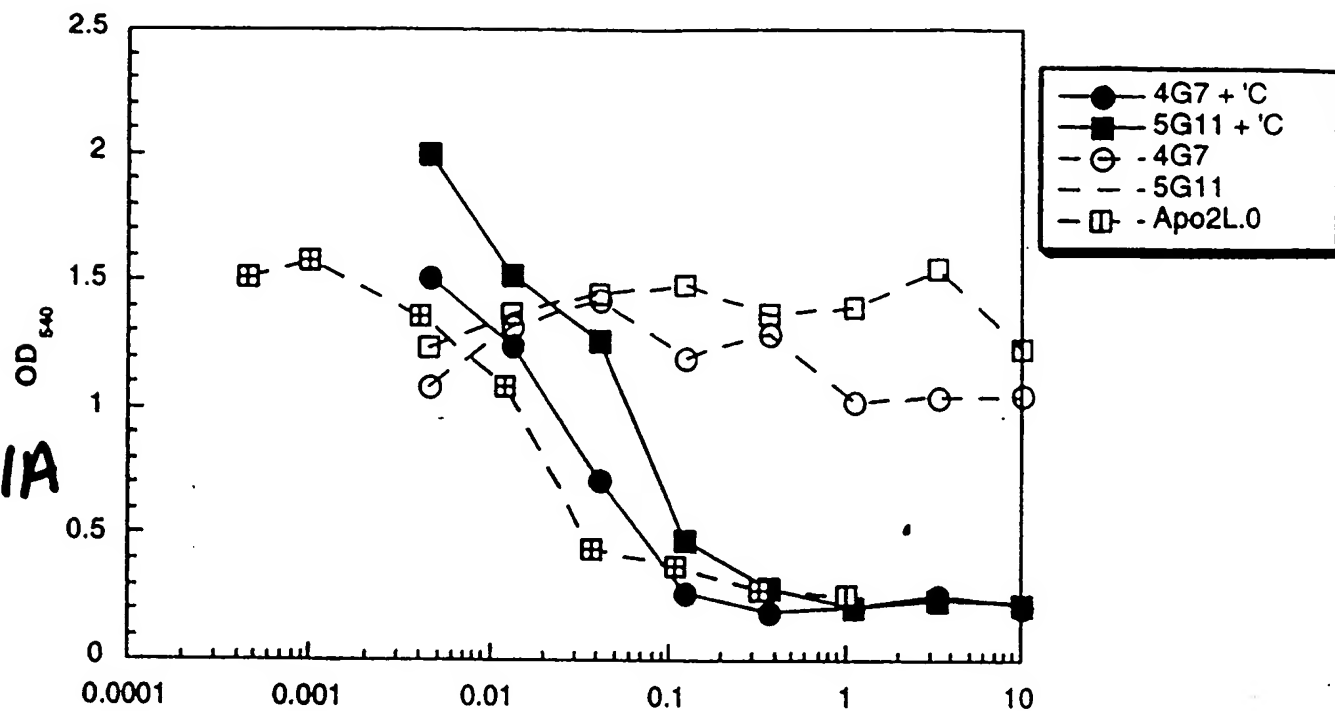


Apoptosis of anti DR4 mAbs plus goat anti FcAb



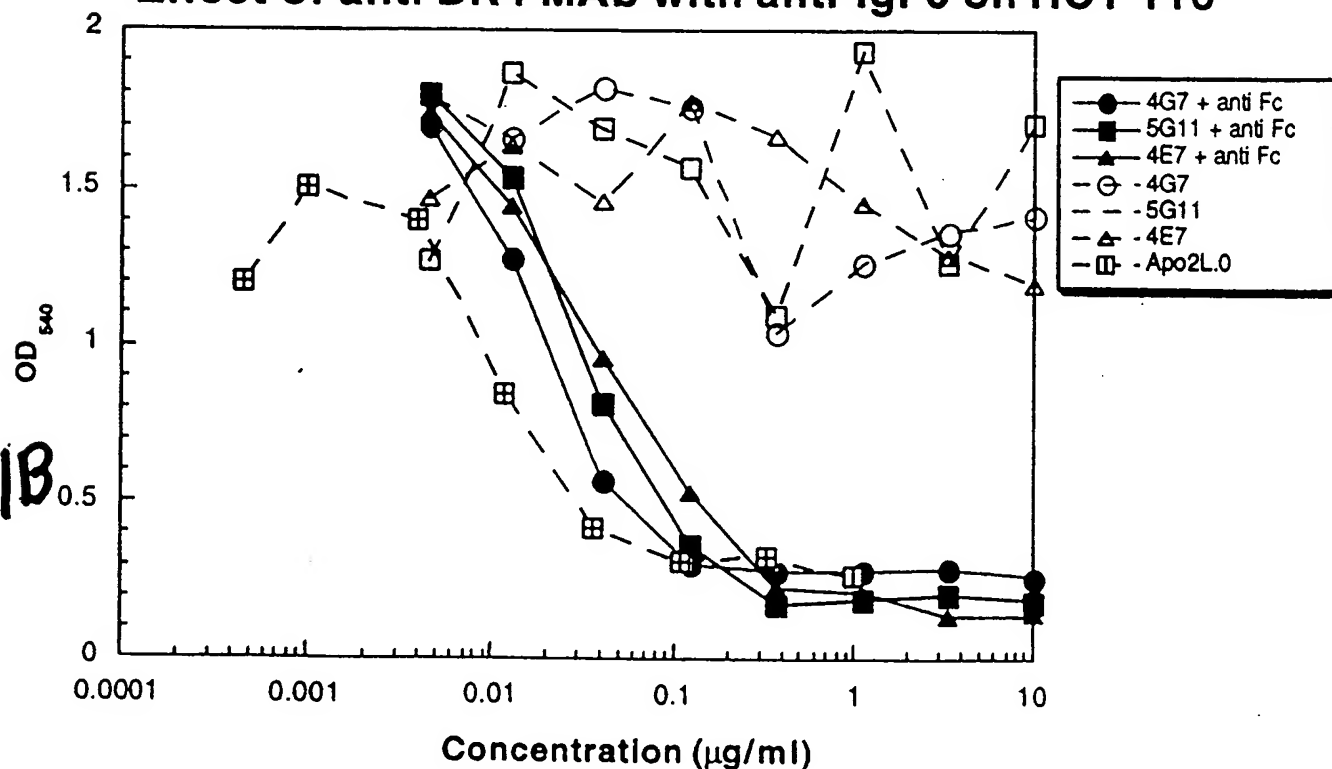
Effect of anti DR4 MAb with complement on HCT 116

Fig. IIA



Effect of anti DR4 MAb with anti-IgFc on HCT 116

Fig. IIB



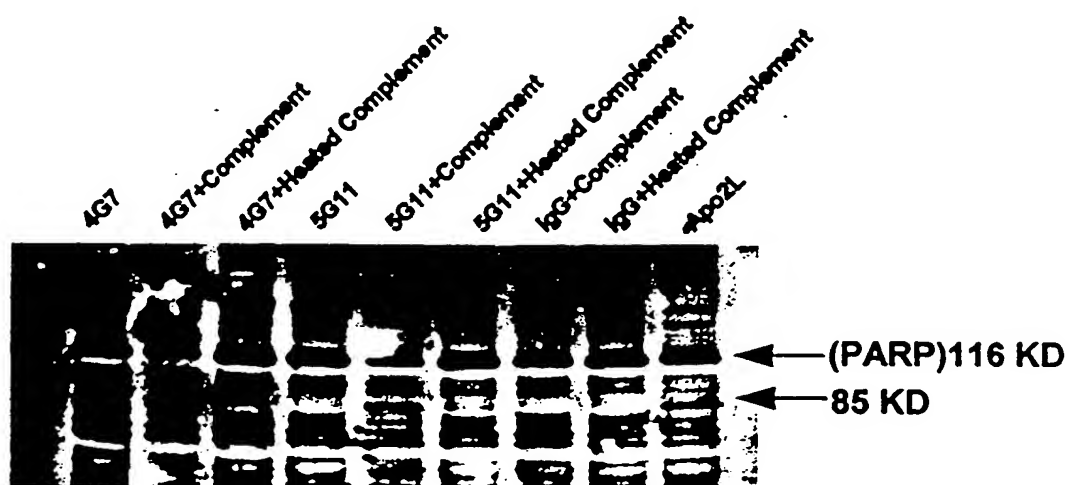


Fig. 12

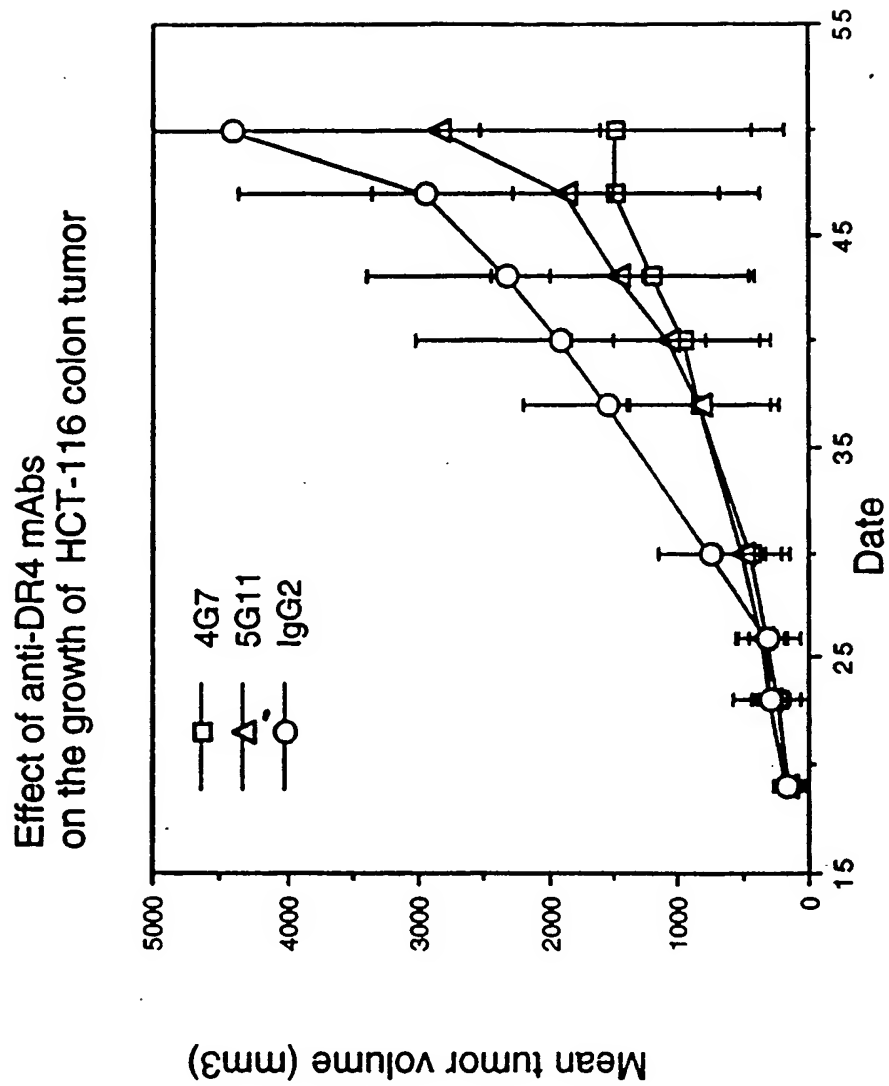


Fig. 13

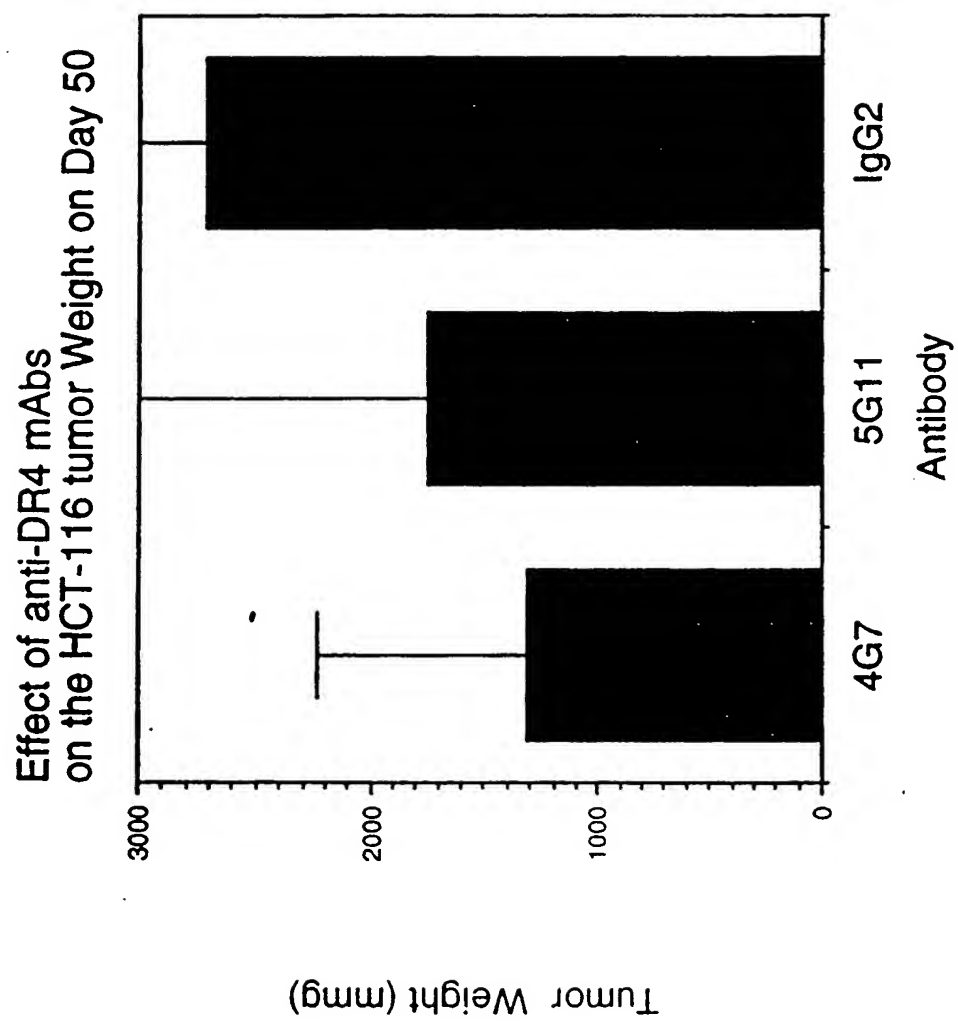


Fig. 14

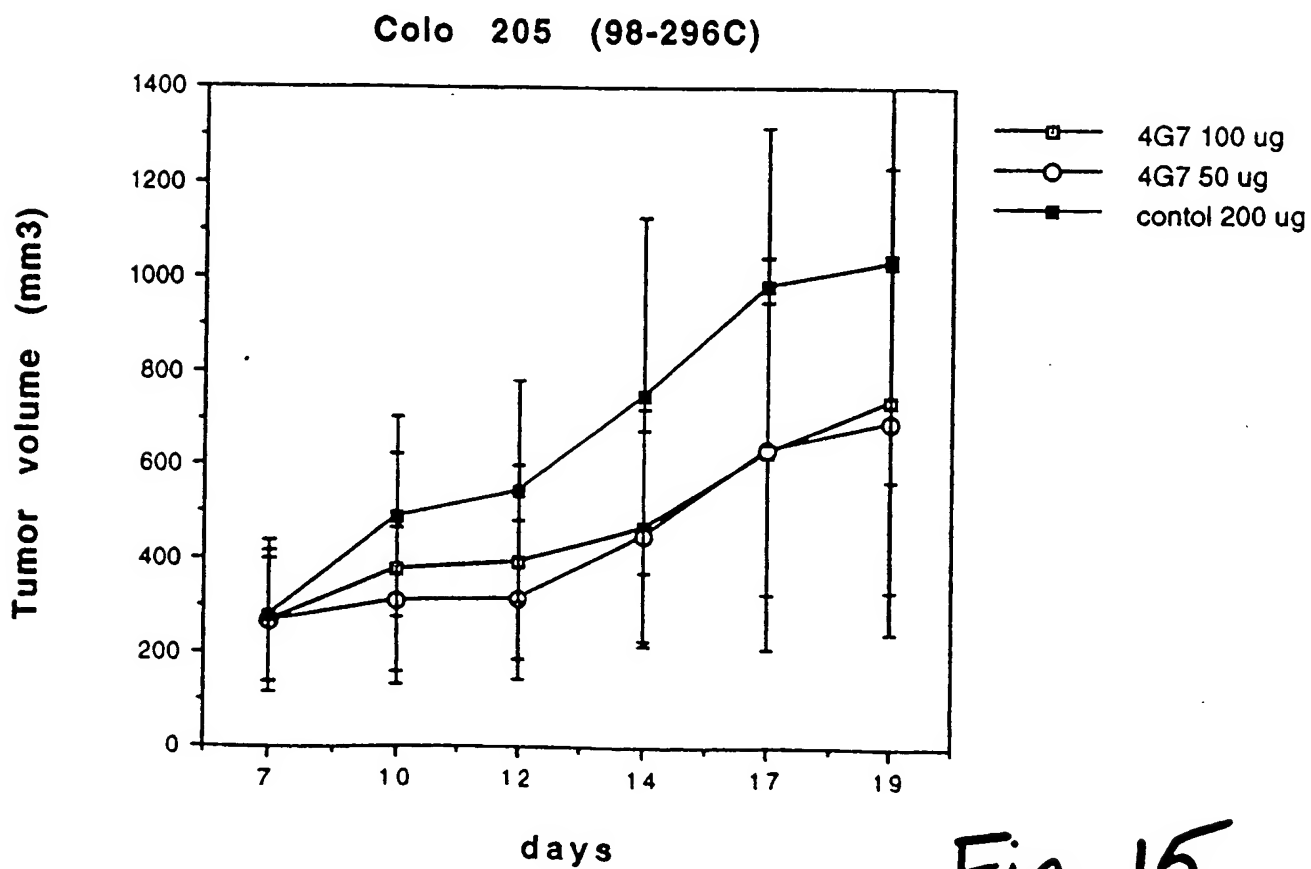
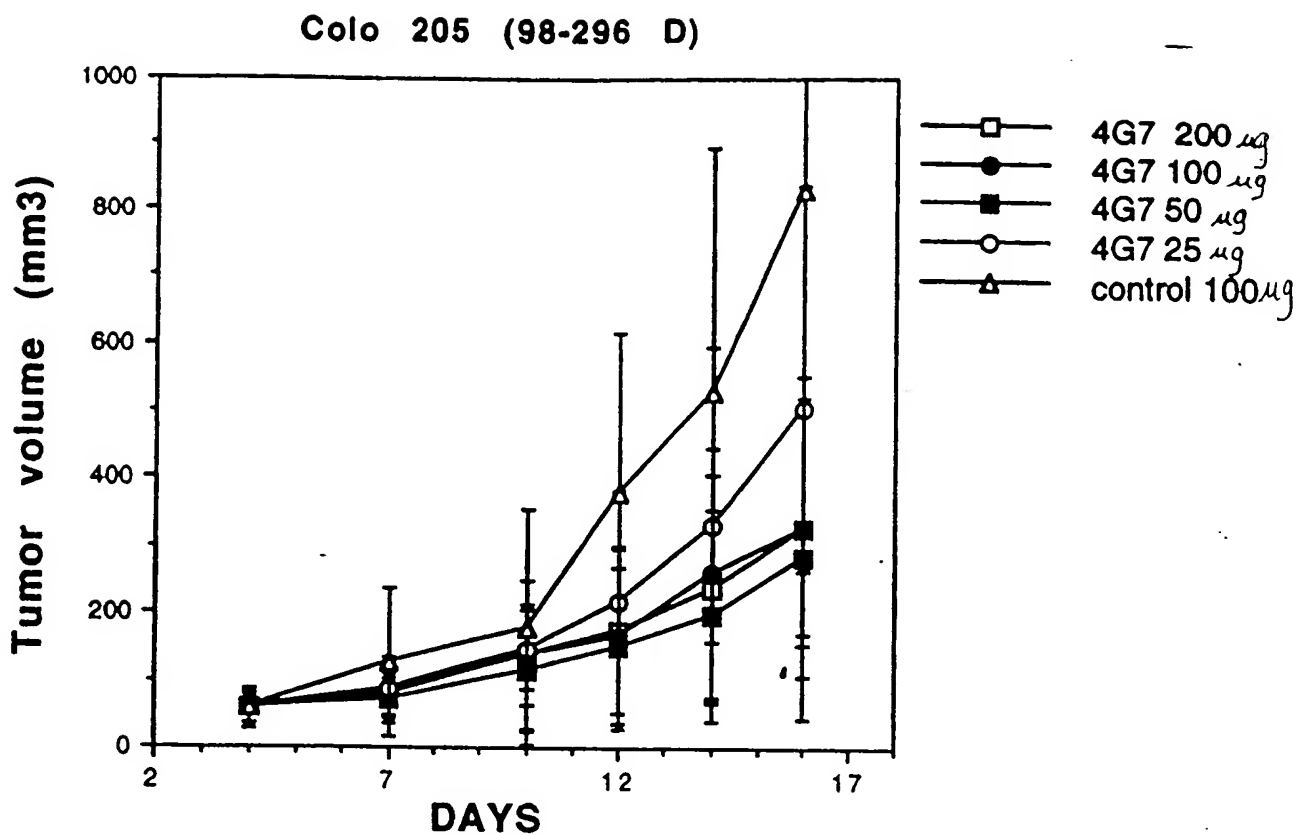


Fig. 15

Colo 205 (98-296 D)

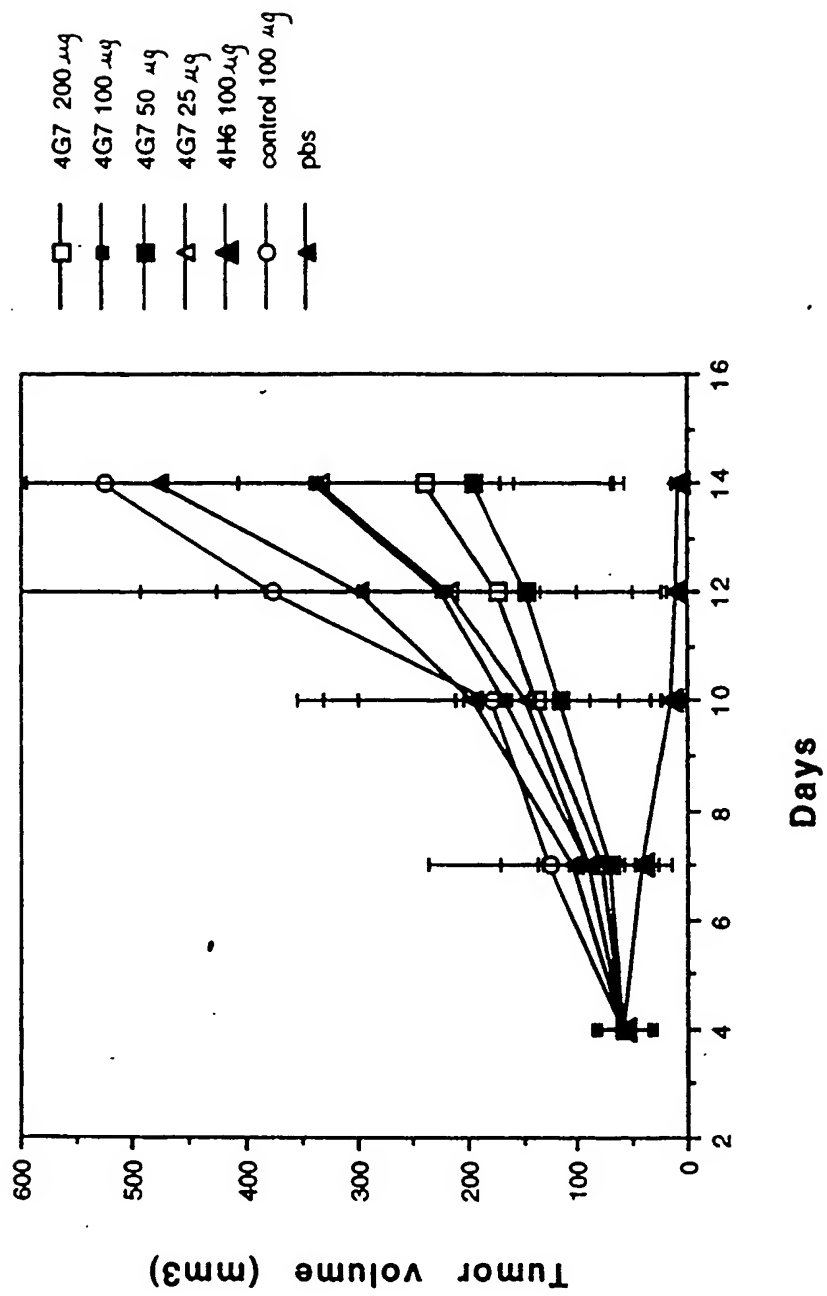


Fig. 16

General Characteristics of Anti-DR4 mAbs

	Isotype	Kd-1 (pM)	Apop w/o L	Apop + &Fc	Apop + C'	Block	Cross reactivity			
							DR4	DR5	DCR1	DCR2
1H5.24.9	IgG2a		-	-	-	ND	+++	-	-	-
1H8.17.5	IgG1		+	+	ND	ND	+++	-	-	-
3G1.17.2	IgG1		-	-	ND	-	+++	-	-	-
4E7.24.3	IgG1	2	+/-	+	-	-	+++	+	-	+/-
4G7.18.8	IgG2a		+/-	+	+	-	+++	-	-	-
4H6.17.8	IgG1	5	+/-	+	-	+	+++	+	-	-
4G10.20.6	IgG1		+	+	ND	-	+++	+	-	-
5G11.17.1	IgG2b	22	+	+	+	ND	+++	++	-	-

All these mAbs recognize DR4 on 9D cells and immune precipitate DR4-IgG.

w/o L : The apoptotic ability of mAbs by themselves was detected on 9D cells, skmes cells , HCT116 and colo 205

+ &FC: The apoptotic ability of mAbs was determined in combination with goat anti-mouse IgG FC.

+ C' : The apoptotic ability of mAbs was determined in the presence of rabbit complement

Degrees of binding (+) to DR5 by Mabs 4E7 and 4H6 at 10 ug/ml are 15% of the binding to DR4.

Fig . 17

```

< 4H6ApDR1
< 4H6 Anti DR4, Murine variable, Human kappaconstant
< ELEMENT: Component (start: 1557/1559; end: 5390/5390)
< length: 702

929 AT GGGATGGTCA TGTATCATCC TTTTCTAGT AGCAACTGCA
    TA CCCTACCAAGT ACATAGTAGG AAAAAGATCA TCGTTGACGT
    1 M G W S C I I L F L V A T A
      ^Signal Sequence

971 ACTGGAGTAC ATTCAGATAT CCAGATGACA CAGACTACAT CCTCCCTGTC
    TGACCTCATG TAAGTCTATA GGTCTACTGT GTCTGATGTA GGAGGGACAG
    15 T G V H S D I Q M T Q T T S S L S
      ^D is first amino acid of variable

1021 TGCCTCTCTG GGAGACAGAG TCACCATCAG TTGCAGGGCA AGTCAGGACA
    ACGGAGAGAC CCTCTGTCTC AGTGGTAGTC AACGTCCCGT TCAGTCCTGT
    32 A S L G D R V T I S C R A S Q D I

1071 TTAGCAATTA TTAAACTGG TATCAGCGGA AACCAGATGG AACTGTTAAA
    AATCGTTAAT AAATTGACC ATAGTCGCCT TTGGTCTACC TTGACAATTT
    49 S N Y L N W Y Q R K P D G T V K

1121 CTCCTGATCT ACTACACATC ACGATTACAC TCAGGAGTCC CATCACGGTT
    GAGGACTAGA TGATGTGTAG TGCTAATGTG AGTCCTCAGG GTAGTGCCAA
    65 L L I Y Y T S R L H S G V P S R F

      CDR1          CDR1          CDR1          CDR1
      FR1          FR1          FR2          FR2
      FR2          CDR2          FR3

```

Fig. 18A

1171	CAGTGGCAGT	GGGTCTGGAA	CAGATTATTC	TCTCACCATT	AGCAACCTGG
	GTCACCGTCA	CCCAGACCTT	GTCTAATAAG	AGAGTGGTAA	TCGTTGGACC
82	S G S	G S G T	D Y S	L T I	S N L E
<hr/>					
1221	AACAAGAAGA	TATTGCCACT	TACTTTGCC	AACAGGGTAA	TACGCTTCCA
	TTGTTCTTCT	ATAACGGTGA	ATGAAAACGG	TTGTCCCAT	ATGCGAAGGT
99	Q E D	I A T	Y F C Q	Q G N	T L P
<hr/>					
			FR3	CDR3	
<hr/>					
1271	TTCACGTTG	GCTCGGCCAC	CAAGCTGGAA	CTAACTCGGA	CCGTGGCTGC
	AAGTGCAAGC	CGAGCCGGTG	GTTCGACCTT	GATTGAGCCT	GGCACCCGACG
115	F T F G	S A T	K L E	L T R T	V A A
<hr/>					
			FR4	CHI	
<hr/>					
1321	ACCATCTGTC	TTCATCTTCC	CGCCATCTGA	TGAGCAGTTG	AAATCTGGAA
	TGGTAGACAG	AAGTAGAAGG	GCGGTAGACT	ACTCGTCAAC	TTAGACCTT
132	P S V	F I F P	P S D	E Q L	K S G T
<hr/>					
			CHI		
<hr/>					
1371	CTGCCCTCTGT	TGTGTGCCTG	CTGAATAAAT	TCTATCCCAG	AGAGGCCAAA
	GACGGAGACA	ACACACGGAC	GACTTATTGA	AGATAGGGTC	TCTCCGGTTT
149	A S V	V C L	L N N F	Y P R	E A K
<hr/>					
			CHI		
<hr/>					
1421	GTACAGTGA	AGGTGGATAA	CGCCCTCCAA	TCGGGTAAT	CCCAGGAGAG
	CATGTCACCT	TCCACCTATT	GCGGGAGGTT	AGCCCATTGA	GGTCCCTCTC
165	V Q W K	V D N	A L Q	S G N S	Q E S
<hr/>					
			CHI		
<hr/>					
1471	TGTCACAGAG	CAGGACAGCA	AGGACAGCAC	CTACAGCCTC	AGCAGCACCC
	ACAGTGTCTC	GTCCTGTCGT	TCCTGTCTGT	GATGTCGGAG	TCGTCTGTGGG
182	V T E	Q D S K	D S T	Y S L	S S T L
<hr/>					
			CHI		
<hr/>					
1521	TGACGCTGAG	CAAAGCAGAC	TACGAGAAAC	ACAAAGTCTA	CGCCTGCGAA

Fig. 18B

199	ACTGCGACTC	GTTTCGCTCTG	ATGCTCTTTG	TGTTTCAGAT	GCGACGCTT												
	T	L	S	K	A	D	Y	E	K	H	K	V	Y	A	C	E	
	CHI																
1571	GTCACCCATC	AGGGCCCTGAG	CTCGCCCGTC	ACAAAGAGCT	TCAACAGGGG												
	CAGTGGGTAG	TCCCGGACTC	GAGCGGGCAG	TGTTTCTCGA	AGTTGTCCCC												
215	V	T	H	Q	G	L	S	S	P	V	T	K	S	F	N	R	G
	CHI																
1621	AGAGTGTTAA	TCTCACAATT															
232	E	C	O														

Fig. 18C

< humanized MaE11 version 1 HEAVY CHAIN
 < 4H6 Anti DR4, murine variable, Human IgG1 heavy constant
 < 4H6Amonomer
 < length: 1431

930 A TGGGATGGTC ATGTATCATC CTTTCTTAG TAGCAACTGC
 T ACCCTACCAG TACATAGTAG GAAAAAGATC ATCGTTGACG
 1 M G W S C I I L F L V A T A
 ^ signal sequence

971 AACTGGAGTA CATTCAGAAG TTCAGCTGAA GGAGTCAGGA CCTGGCCTGG
 TTGACCTCAT GTAAGTCTTC AAGTCGACTT CCTCAGTCCT GGACCGGACC
 15 T G V H S E V Q L K E S G P G L V
 ^E is amino acid 1 of variable heavy

FR1

1021 TGGCGCCCTC ACAGAGCCTG TCCATCACTT GCACTGTCTC TGGGTTTCA
 ACCGCGGGAG TGTCTCGGAC AGGTAGTGAA CGTGACAGAG ACCCAAAAGT
 32 A P S Q S L S I T C T V S G F S

FR1

1071 TTAACCAGCT ATGGTGATACA CTGGGTTTCG CAGCCTCCAG GAAAGGGTCT
 AATTGGTCGA TACCACATGT GACCCAAGCG GTCGGAGGTC CTTTCCCAGA
 48 L T S Y G V H W V R Q P P G K G L

CDR1

FR2

1121 GGAGTGGCTG GGAGTAATAT GGGCTGTTGG AAGCACAAAT TATAATTCGG
 CCTCACCGAC CCTCATATATA CCCGACAACC TTCGTGTTTA ATATTAAGCC
 65 E W L G V I W A V G S T N Y N S A

FR2

CDR2

1171 CTCTCATGTC CAGACTGAGC ATCAGCAAAG ACAACTCCAA GAGCCAAGTT

Fig. 18D

82	GAGAGTACAG	GTCTGACTCG	TAGTCGTTTC	TGTTGAGGTT	CTCGGTTCAA
	L M S	R L S	I S K D	N S K	S Q V
	<u>CDR2</u>				
	<u>FR3</u>				
1221	TTCTTAAAA	TGAACAGTCT	GCAAACCTGAT	GACACAGCCA	TGTACTACTG
	AAGAATTTT	ACTTGTCAGA	CGTTTGACTA	CTGTGTCGGT	ACATGATGAC
98	F L K M	N S L	Q T D	D T A M	Y Y C
	<u>FR3</u>				
1271	TGCCAGAGAG	GGGGAATTCT	ATTACTACGG	TAGTAGTCTC	CTATCTTACC
	ACGGTCTCTC	CCCCTTAAGC	TAATGATGCC	ATCATCAGAG	GATAGAATGG
115	A R E	G E F D	Y Y G	S S L	L S Y H
	<u>FR3</u>				
	<u>CDR3</u>				
1321	ATTCTATGAA	CTTCTGGGGT	CAAGGAACCT	CAGTCACCGT	CTCCTCAGCC
	TAAGATACTT	GAAGACCCCA	GTTCCCTTGA	GTCAGTGGCA	GAGGAGTCGG
132	S M N	F W G	Q G T S	V T V	S S A
	<u>CDR3</u>				
	<u>FR4</u>				
	<u>CHI</u>				
1371	AAAACGACGG	GCCCATCGGT	CTTCCCCCTG	GCACCCCTCT	CCAAGAGCAC
	TTTGTCTGCC	CGGGTAGCCA	GAAGGGGGAC	CGTGGGAGGA	GTTCTCTGTG
148	K T T G	P S V	F P L	A P S S	K S T
	<u>CHI</u>				
1421	CTCTGGGGGC	ACAGCGGGCC	TGGCTGCCT	GGTCAAGGAC	TACTTCCCCG
	GAGACCCCGG	TGTCGCCGGG	ACCCGACGGA	CCAGTTCCTG	ATGAAGGGGC
165	S G G	T A A L	G C L	V K D	Y F P E
	<u>CHI</u>				
1471	AACCGGTGAC	GGTGTCGTGG	AACTCAGGCG	CCCTGACCAG	CGGCGTGCAC
	TTGGCCACTG	CCACAGCACC	TTGAGTCCGC	GGGACTGGTC	GCCGCACGTG
182	P V T	V S W	N S G A	L T S	G V H
	<u>CHI</u>				

Fig. 18E

1521	ACCTTCCCG	CTGTCCTACA	GTCCTCAGGA	CTCTACTCCC	TCAGCAGCGT
	TGGAAGGGCC	GACAGGATGT	CAGGAGTCCT	GAGATGAGGG	AGTCGTGCGA
198	T F P A	V L Q	S S G	L Y S L	S S V
	<i>CH1</i>				
1571	GGTGACTGTG	CCCTCTAGCA	GCTTGGGCAC	CCAGACCTAC	ATCTGCAACG
	CCACTGACAC	GGGAGATCGT	CGAACCCCGTG	GGTCTGGATG	TAGACGTTGC
215	V T V	P S S	L G T	Q T Y	I C N V
	<i>CH1</i>				
1621	TGAATCACAA	GCCCAGCAAC	ACCAAGGTGG	ACAAGAAAGT	TGAGCCCCAA
	ACTTAGTGTT	CGGGTCGTTG	TGGTTCCACC	TGTTCTTTCA	ACTCGGGTTT
232	N H K	P S N	T K V	D K K V	E P K
	<i>CH1</i>				
1671	TCTTGTGACA	AAACTCACAC	ATGCCCCACCG	TGCCCCAGCAC	CTGAACCTCT
	AGAACACTGT	TTTGAGTGTG	TACGGGTGGC	ACGGGTCTGTG	GACTTGAGGA
248	S C D K	T H T	C P P	C P A P	E L L
	<i>CH1</i>				
1721	GGGGGACCG	TCAGTCTTCC	TCTTCCCCCC	AAAACCCCAAG	GACACCCCTCA
	CCCCCTGGC	AGTCAGAAAG	AGAAGGGGGG	TTTTGGGTTT	CTGTGGGAGT
265	G G P	S V F L	F P P	K P K	D T L M
	<i>CH2</i>				
1771	TGATCTCCCG	GACCCCTGAG	GTCACATGCG	TGGTGGTGGA	CGTGAGCCAC
	ACTAGAGGGC	CTGGGGACTC	CAGTGTACGC	ACCACCACCT	GCACTCGGTG
282	I S R	T P E	V T C V	V V D	V S H
	<i>CH2</i>				
1821	GAAGACCCTG	AGGTCAAGTT	CAACTGGTAC	GTGGACGGCG	TGGAGGTGCA
	CTTCTGGGAC	TCCAGTTCAA	GTTGACCATG	CACCTGCCCG	ACCTCCACGT
298	E D P	E V K F	N W Y	V D G V	E V H
	<i>CH2</i>				
1871	TAATGCCAAG	ACAAAGCCGC	GGGAGGAGCA	GTACAACAGC	ACGTACCGGG
	ATTACGGTTC	TGTTTCGGCG	CCCTCCTCGT	CATGTTGTCG	TGCATGGCCC
315	N A K	T K P R	E E Q	Y N S	T Y R V
	<i>CH2</i>				

Fig. 18F

1921 TGGTCAGCGT CCTCACCCTC CTGCACCAGG ACTGGCTGAA TGGCAAGGAG
 ACCAGTCGCA GGAGTGGCAG GACGTGGTCC TGACCGACTT ACCGTTCCTC
 332 V S V L T V L H Q D W L N G K E
 CH2
 1971 TACAAAGTGA AGGTCTCCAA CAAAGCCCTC CCAGCCCCCA TCGAGAAAAC
 ATGTTACAGT TCCAGAGGTT GTTTCGGGAG GGTCGGGGGT AGCTCTTTTG
 348 Y K C K V S N K A L P A P I E K T
 CH2
 2021 CATCTCCAAA GCCAAAGGGC AGCCCCGAGA ACCACAGGTG TACACCCCTGC
 GTAGAGGTTT CGGTTTCCCG TCGGGGCTCT TGGTGTCCAC ATGTGGGACG
 365 I S K A K G Q P R E P Q V Y T L P
 CH2
 2071 CCCCATCCCG GGAAGAGATG ACCAAGAACC AGGTCAGCCT GACCTGCCTG
 GGGTAGGGC CCTTCTCTAC TGGTTCCTGG TCCAGTCGGA CTGGACGGAC
 382 P S R E E M T K N Q V S L T C L
 CH3
 2121 GTCAAAGGCT TCTATCCAG CGACATCGCC GTGGAGTGG AGAGCAATGG
 CAGTTTCCGA AGATAGGGTC GCTGTAGCGG CACCTCACCC TCTCGTTACC
 398 V K G F Y P S D I A V E W E S N G
 CH3
 2171 GCAGCCGGAG AACAACTACA AGACCAAGCC TCCCGTGCTG GACTCCGACG
 CGTCGGCCTC TTGTTGATGT TCTGGTGCGG AGGGCACGAC CTGAGGCTGC
 415 Q P E N N Y K T T P P V L D S D G
 CH3
 2221 GCTCCTTCTT CCTCTACAGC AAGCTCACCG TGGACAAGAG CAGGTGGCAG
 CGAGGAAGAA GGAGATGTCG TTCGAGTGCC ACCTGTTCTC GTCCACCGTC
 432 S F F L Y S K L T V D K S R W Q
 CH3
 2271 CAGGGGAACG TCTTCTCATG CTCCGTGATG CATGAGGCTC TGCACAACCA
 GTCCCTTGC AGAAGAGTAC GAGGCACTAC GTACTCCGAG ACGTGTGGT

Fig. 186

448	Q	G	N	V	F	S	C	S	V	M	H	E	A	L	H	N	H
	<i>CH3</i>																
2321	CTACACGCAG AAGAGCCTCT CCTGTCTCC GGTAAATGA																
	GATGTGCGTC TTCTCGGAGA GGGACAGAGG CCCATTACT																
465	Y	T	Q	K	S	L	S	L	S	P	G	K	O				
	<i>CH3</i>																

Fig. 18 H

SKMES

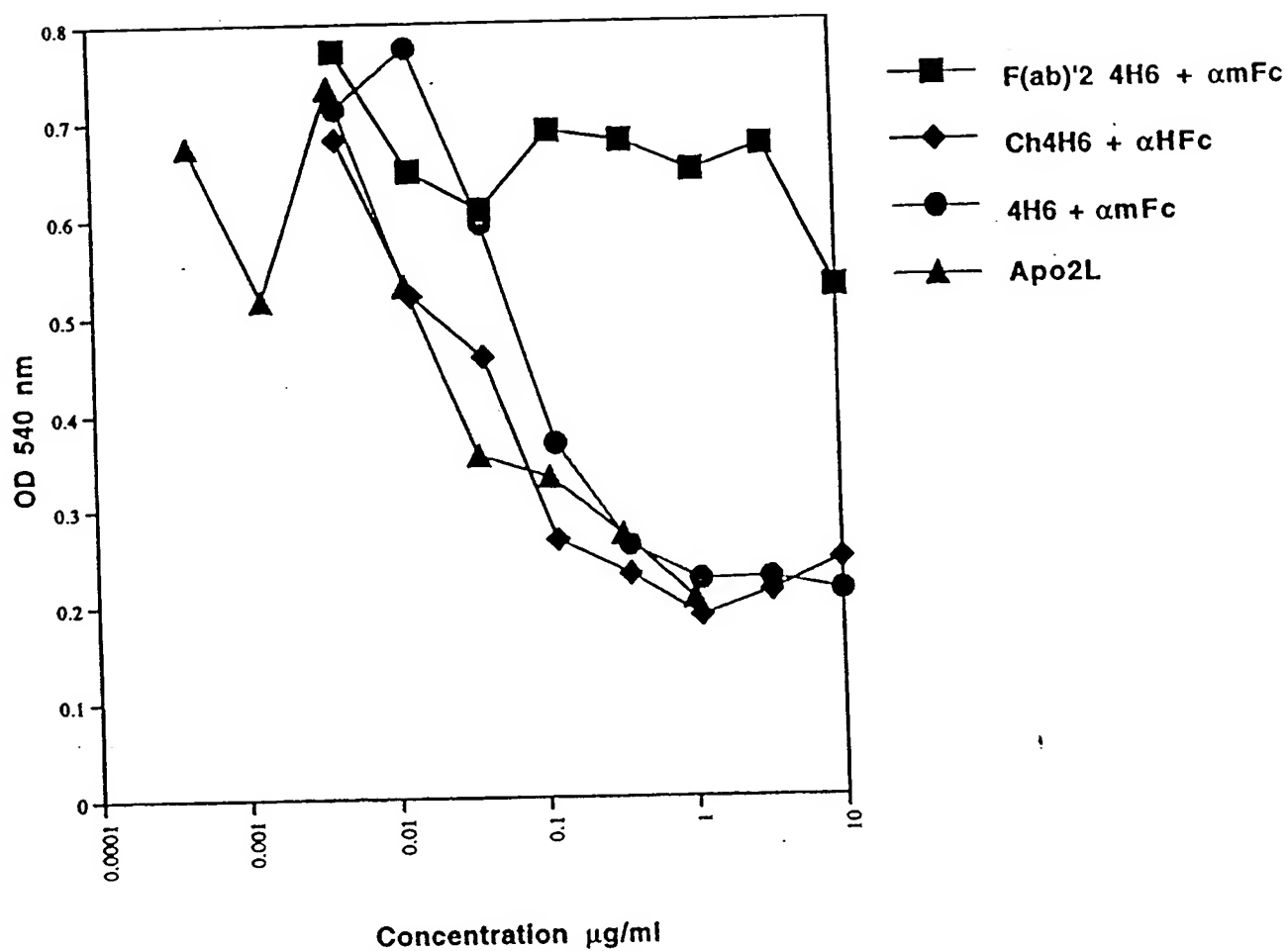


Fig. 19

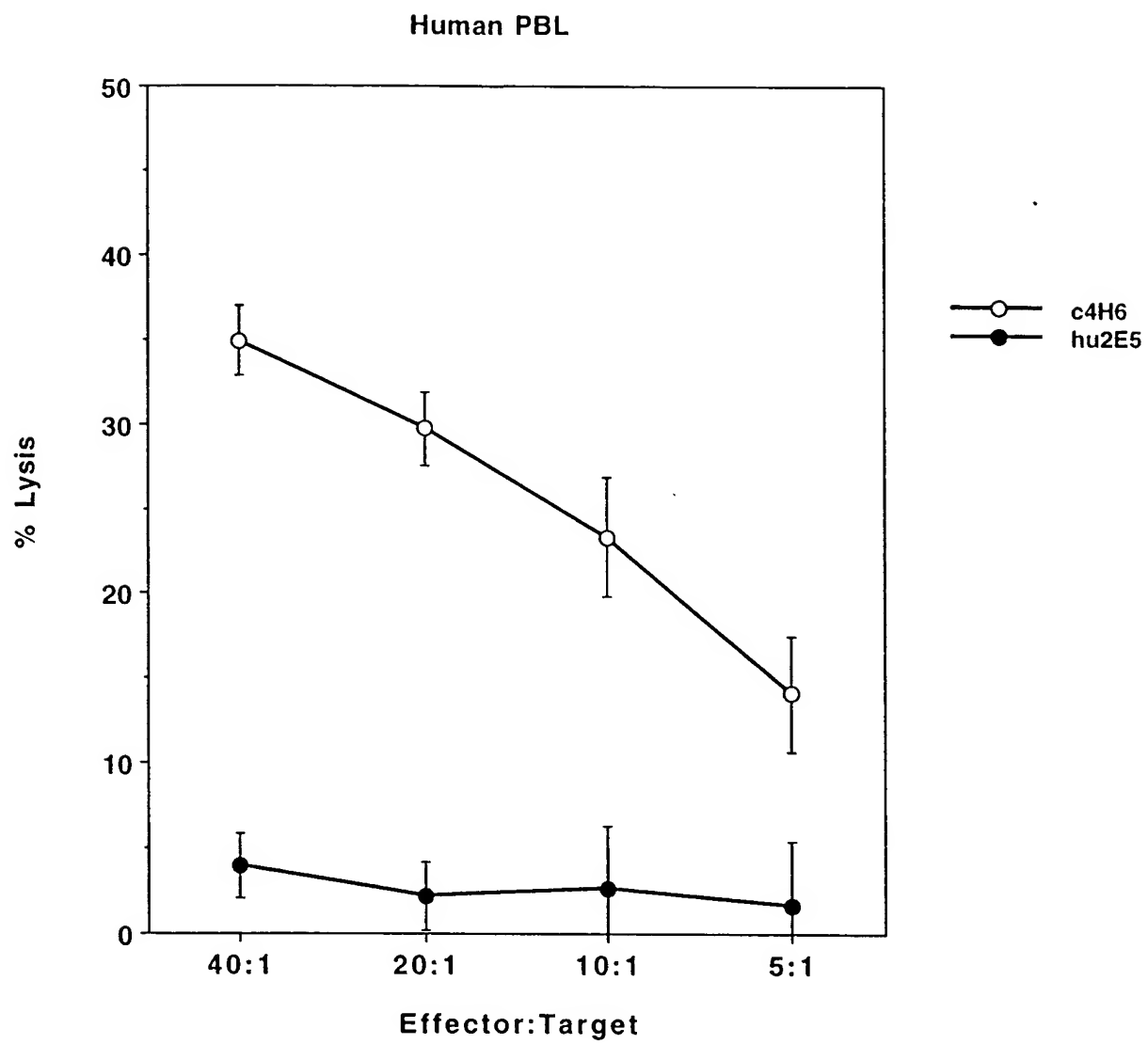


Fig. 20

Comparison of the in vivo efficacy of Murine and Chimera 4H6

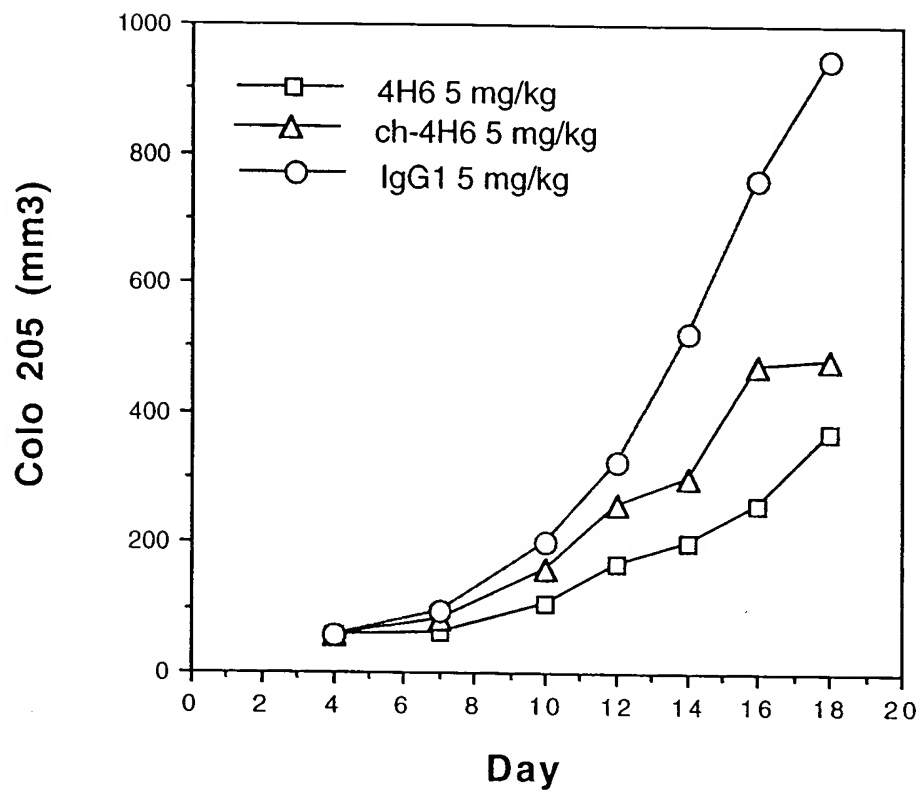


Fig. 21